## (19) World Intellectual Property **Organization**

International Bureau





(43) International Publication Date 2 October 2003 (02.10.2003)

PCT

English

## (10) International Publication Number WO 2003/080580 A3

(51) International Patent Classification<sup>7</sup>: C07D 215/40, A61K 31/47, A61P 25/00, C07D 487/04, 487/08

(21) International Application Number:

PCT/EP2003/003197

(22) International Filing Date: 25 March 2003 (25.03.2003)

(25) Filing Language:

(26) Publication Language: English

(30) Priority Data:

0207289.0 27 March 2002 (27.03.2002) GB0225678.2 4 November 2002 (04.11.2002) GB

(71) Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 ONN (GB).

(72) Inventors; and

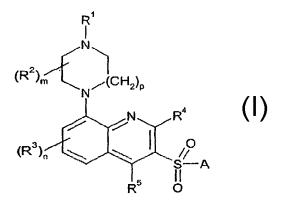
(75) Inventors/Applicants (for US only): AHMED, Mahmood [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). JOHNSON, Christopher, Norbert [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). JONES, Martin, C [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). MACDONALD, Gregor, James [GB/GB];

GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). MOSS, Stephen, Frederick [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). THOMPSON, Mervyn [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). WADE, Charles, Edward [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). WITTY, David [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).

- (74) Agent: VALENTINE, Jill, Barbara; GlaxoSmithKline, CN925.1, 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

[Continued on next page]

(54) Title: QUINOLINE DERIVATIVES AND THEIR USE AS 5-HT6 LIGANDS



2003/080580 A3 ||||||||| (57) Abstract: The present invention relates to quinoline compounds of formula (I) or a pharmaceutically acceptable salt thereof, wherein R<sup>1</sup> and R<sup>2</sup> independently represent hydrogen or C<sub>1.6</sub> alkyl or R<sup>1</sup> is linked to R<sup>2</sup> to form a group (CH<sub>2</sub>)<sub>2</sub>, (CH<sub>2</sub>)<sub>3</sub> or (CH<sub>2</sub>)<sub>4</sub>; R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> independently represent hydrogen, halogen, cyano, -CF<sub>3</sub>, -CF<sub>3</sub>O, C<sub>1.6</sub> alkyl, C<sub>1.6</sub> alkoxy, C<sub>1.6</sub> alkoxy, or a group -CONR<sup>6</sup>R<sup>7</sup>; m represents an integer from 1 to 4, such that when m is an integer greater than 1, two R<sup>2</sup> groups may instead be linked to form a group CH<sub>2</sub>, (CH<sub>2</sub>)<sub>2</sub> or (CH<sub>2</sub>)<sub>3</sub>; n represents an integer from 1 to 3; p represents 1 or 2; A represents a group -Ar<sup>1</sup> or -Ar<sup>2</sup>Ar<sup>3</sup>; Ar<sup>1</sup>, Ar<sup>2</sup> and Ar<sup>3</sup> independently represent and aryl group or a heteroaryl group, both of which may be optionally substituted by one or more substituents having pharmacological activity, to processes for their preparation, to compositions containing them and to their use in the treatment of CNS and other disorders.



# WO 2003/080580 A3



European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

with international search report

(88) Date of publication of the international search report: 5 February 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

## INTERNATIONAL SEARCH REPORT

Interna I Application No PCT, L. 03/03197

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07D215/40 A61K C07D487/04 C07D487/08 A61P25/00 A61K31/47 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 CO7D A61K A61P Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category 5 1,22-24WO 99 65906 A (ALLELIX BIOPHARMACEUTICALS Α INC.) 23 December 1999 (1999-12-23) cited in the application claims WO 00 63203 A (ALLELIX BIOPHARMACEUTICALS 1,22-24A INC.) 26 October 2000 (2000-10-26) claims Patent family members are listed in annex. Further documents are listed in the continuation of box C. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-O document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 12/11/2003 29 October 2003 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016 Van Bijlen, H

### INTERNATIONAL SEARCH REPORT

nt ional application No. CT/EP 03/03197

Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) Box I This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claims 27-28 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. 2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet) This International Searching Authority found multiple inventions in this international application, as follows: As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: The additional search fees were accompanied by the applicant's protest. Remark on Protest No protest accompanied the payment of additional search fees.

## **INTERNATIONAL SEARCH REPORT**

PCT/LI 03/03197

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9965906	A	23-12-1999	US AT AU CA WO EP JP	6251893 B1 251163 T 765256 B2 4253199 A 2335285 A1 9965906 A1 1105393 A1 2003523922 T	26-06-2001 15-10-2003 11-09-2003 05-01-2000 23-12-1999 23-12-1999 13-06-2001 12-08-2003
WO 0063203	A	26-10-2000	WO AU CA EP JP	0063203 A1 3403599 A 2370147 A1 1173432 A1 2002542241 T	26-10-2000 02-11-2000 26-10-2000 23-01-2002 10-12-2002